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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	21

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/826,361	Applicant(s) Mosselman et al.
	Examiner Michael Pak	Group Art Unit 1646

X Responsive to communication(s) filed on *May 1, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *1-12 and 14-19* is/are pending in the application.

Of the above, claim(s) *9-11, 14, and 18* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

X Claim(s) *1-8, 12, and 15-17* is/are rejected.

X Claim(s) *19* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Amendment filed 1 May 2000 (Paper No. 18) has been received and entered.

2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

3. Applicant's arguments filed 1 May 2000 (Paper No. 18) have been fully considered but they are not found persuasive.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

5. Claim 19 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Accordingly, the claim 19 has not been further treated on the merits.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 6-8, 12, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a protein comprising SEQ ID NO: 5, 6, 21, or 25, does not reasonably provide enablement for,

A) an isolated DNA encoding a protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain, wherein the amino acid sequence of said DNA-binding domain of said protein exhibits at least 80% or 90% homology with the amino acid sequence of SEQ ID NO:3 and the amino acid sequence of said ligand binding domain of said protein exhibits at least 70% or 75% homology with the amino acid sequence of SEQ ID NO:4;

B) a recombinant expression vector comprising the isolated DNA of A) above;

C) a cell transfected with the DNA of A) above or the recombinant expression vector of B) above; and

D) a DNA of claim 12 encoding a chimeric protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-3 and 12 encompass an isolated DNA encoding a variant protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain without a functional limitation. Claims 6-8 and 15-17 encompass a vector or cell comprising the DNA of claims 1-3. However, the specification fails to teach how to make and use the whole genus of an isolated DNA encoding a variant protein having an N-terminal domain, a DNA binding domain, and a ligand binding domain without a functional limitation. The specification discloses an example of a specific species of human estrogen receptor and its splice variant but does not teach the whole genus of claimed products. It would require undue experimentation to test the function of a variant receptor which has essentially unlimited substitutions because the percent homology with SEQ ID NO: 3 and 4 are not defined and includes gaps and nonconserved substitutions and which includes variant proteins with only the N-terminal domain, a DNA binding domain, and the ligand binding domain. One skilled in the art cannot substitute amino acid randomly and predictably get functional protein (Bowie et al., Science, 1990). For example the receptor variants have other linkers or domains other than the N-terminal domain, a DNA binding domain, and the ligand binding domain which provide proper tertiary structural folding which is required for proper ligand binding function and transcriptional activation. Furthermore, the claims encompass

variant proteins with large deletions in a domain which is essential for function. Thus, the claims encompass a genus of large number of DNAs which encode non-functional receptors. The vector of claim 6 and the host cell transfected with the vector of claim 6 comprise the DNA of claim 1 and thus encompass the same genus of large number of DNAs which encode non-functional receptors.

Claims 7 and 8 encompass a cell transfected with DNA of claim 1 which is not in a vector. However, the specification does not teach how to transfect cell with DNA which is not in a vector. One of skilled in the art do not transfect cells with cDNA which are not packaged in a vector because without the vector the expression copies of the DNA is not sufficient for expression of the protein product.

8. Claims 1-3, 6-8, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims encompass the DNA or vectors and cells comprising the DNA encoding a variant protein which is naturally occurring but

not disclosed in the specification nor to one of skilled in the art. Claimed DNA encoding protein variants encompass a large genus of nuclear receptors which are alleles or variants whose function has yet to be identified from different species of animal because the structure of the newly identified naturally occurring receptor is not known. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* held that a generic claim to human or mammalian when only the rat protein sequence was disclosed did not have written description in the specification.

Claim Rejections - 35 USC § 102

9. Claims 1-6 and 15-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Cabib et al.((C); U.S. 5,936,731).

Cabib et al. disclose human chromosome karyotypes (figures 7-11; columns 5, 10, and 33-34).

Claims 1-5 and 15-17 encompass isolated human chromosome because the chromosomes comprises claimed nucleic acid molecules. Since the human genome comprises all the gene sequences the chromosomes inherently comprises the sequences claimed.

Applicants argue that the claimed gene is located on chromosome 14. However, the applicant did not point to the location in the specification which discloses this information. Furthermore, claims are not limited to the species of DNA comprising specific SEQ ID NO: but encompasses a genus of DNA

encoding a domain of the protein with percent identity to a SEQ ID NO:. Furthermore, Cabib et al. disclose the isolated human chromosome 14.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 1-8 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cabib et al.(C) in view of Kausch et al.(A); U.S. '164).

Applicants argue that Kausch differs from the present invention in that it discloses a method for the isolation and sorting of chromosomes in general and is not concerned with the

DNA per se, whereas the present invention relates to the cloning of a particular DNA and its use in medical research. However, the claims do not exclude the chromosomal DNA disclosed in Kausch et al. and the claims are not limited to the cloning of a particular DNA and its use in medical research.

Applicants argue that the teaching disclosed in Kausch et al. is nothing more than a general teaching about hypothetical uses of the method and can by no means be interpreted as a specific teaching for the isolation and cloning of ER-beta DNA. However, as discussed in the last office action, the chromosomal DNA inherently comprises the DNA claimed and thus anticipates the claims. Applicants further argue that if this would be the case, then for the same reasons applied to Kausch et al. rejection, the Maniatis Laboratory Manual of Cloning would have anticipated all nucleotide sequences that haven been cloned subsequent to its publication. However, Kausch et al. anticipates the claims as discussed above because the chromosomal DNA is disclosed. Whether Maniatis anticipates the present claims has not previously addressed. If Maniatis discloses the human chromosomal DNA, the claims will be anticipated by the reference.

Applicants argue that Kausch et al. Teaching in Example 2 concerns the isolation and sorting of human chromosome 1 which does not comprise the DNA encoding ER-beta which is located on chromosome 14. However, the Kausch et al. teaches that many

chromosomes can be sorted at once (column 9, lines 29-43), which includes all the chromosomes in the cell.

12. Claim 12 is rejected under 35 U.S.C. 102(b) as being anticipated by Evans et al.((B); U.S. '233).

Evans et al. teach DNA encoding chimeric receptor of nuclear or steroid receptor family members including estrogen receptor and a method of screening for ligands using the chimeric receptors (column 7, lines 19 to column 8, line 31).

Newly amended claim 12 encompasses one of the domains of claim 1 which is the DNA encoding the DNA binding domain of estrogen receptor which is taught by Evans et al. Evans et al. teach the remaining chimeric receptor comprising other domains of nuclear receptors(column 7, lines 19 to column 8, line 31).

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (703) 305-7038. The examiner can normally be reached on Monday through Friday from 5:50 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Michael D. Pak

Michael Pak
Primary Patent Examiner
Art Unit 1646
13 November 2000